Effectiveness of Nonpharmacological Treatment Methods on Multiple Sclerosis compared to Pharmacologic Treatment Methods

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ABSTRACT

Multiple sclerosis is a chronic, progressive, debilitating autoimmune disease. It is generally diagnosed in young adults and at this time is not yet curable. Over time there have been new developments in treatment options and symptom management, but compliance and effectiveness of treatments have been barriers to managing MS. The purpose of this review is to evaluate the efficacy of nonpharmacological methods in managing MS symptoms and disease course compared with the traditional pharmacological methods. The goal is to prove that avoiding triggers of relapse and decreasing relapse frequency using nonpharmacological methods is as effective in preventing disability and maintaining quality of life as taking daily, lifelong medications. Using databases such as EBSCO, CINAHL, PubMed, Medline Plus, and Academic Search Complete a variety of studies including meta-analyses, systematic reviews, and clinical trial results were used to establish a design for best practice in treating and managing MS to provide the best quality of life for patients with multiple sclerosis. The results of this study show that nonpharmacological methods alone are not enough to slow or limit the disease progression. Pharmacological methods have proven to slow the progression of disability but using medication and nonpharmacological practices in tandem show the best outcomes in decreasing and preventing disability.

INTRODUCTION

- Multiple Sclerosis is an autoimmune disorder that causes tissue inflammation and demyelination. (Kakalacheva, 2011)
- Most commonly diagnosed is Relapsing remitting MS (RRMS), but other types include clinically isolated syndrome (CIS), secondary progressive MS (SPMS), and primary progressive MS (PPMS). (Kakalacheva, 2011)
- MS most commonly effects Caucasian women, with average diagnosis between the ages of 20 and 50. However, anyone can be diagnosed with MS. (Kakalacheva, 2011)
- Symptoms of MS include physical disability, pain, sensory disturbances, cognitive difficulties, personality changes, anxiety, depression, and fatigue. (Bol et al., 2012)
- RRMS is characterized by periods of exacerbation and remission of neurologic symptoms.
- Triggers of MS include:
    - Increase in core body temperature induced by exercise or fever
    - Increase in stress/stressful life events
    - Vitamin D deficiency
    - Post-partum periods, unrelated to breastfeeding
    - Smoking and tobacco use have not shown to induce relapses, but they have been proven to increase the speed of disability progression.
    - Viral and bacterial infections when in the setting of gene mutations
        - Most common viruses linked to MS are Epstein Barr Virus, human herpesvirus-6, and varicella-zoster virus
    - Other triggers without strong evidence include age, obesity, elevated lipids, and rheumatoid arthritis

(Kakalacheva, 2011) (Xie et al., 2020)

OBJECTIVES

- Identify triggers of Multiple Sclerosis relapses.
- Determine if avoiding triggers is as effective in preventing relapse as treating pharmacologically long term.
- Determine effectiveness of pharmacologic MS management methods.
- Compare nonpharmacological and pharmacological methods for managing MS and preventing relapses and disability progression.

CLINICAL SCENARIO

F.C. is a 53-year-old woman diagnosed with MS at the age of 28 while pregnant with her second child. At the time her presenting symptom was weakness on the right side of the body including upper and lower extremities. No difficulties with speech or facial paralysis and no history of injury. There was no evidence of stroke, but MRI showed lesions consistent with Multiple sclerosis. At the time she was treated with corticosteroids and with time her symptoms resolved completely. After her pregnancy she resumed smoking cigarettes and drinking alcohol but quit smoking about 5 years later indefinitely. Since her initial symptoms and diagnosis, she has had no further relapse, but brain MRI has shown increased number of lesions. She has not taken any disease modifying medications due to their cost, but does avoid triggers such as tobacco, heat such as hot tubs or hot showers, and manages her stress levels with yoga, therapy, and medication when necessary. F.C. would like to know if it would be beneficial for her to consider taking a disease-modifying drug and if it would make a difference at her age, disease severity, and disease disability scale.

Nonpharmacological Treatment Methods

- Avoid triggers of relapse, most importantly for those with MS is smoking cessation.
    - Smoking cessation can definitively decrease the Multiple Sclerosis Severity Score, which includes disability severity. (Manoucherinia et al., 2013)
- Stress management
    - Cognitive behavioral therapy called stress management therapy for MS (SMT-MS) proved to be effective in stopping new brain lesions from forming, in turn slowing progression of disability and other neurological symptoms. (Mohr et al., 2012)
- Progressive muscle relaxation techniques, exercise, and yoga proved to enhance quality of life in those with MS. (Ghafari et al., 2009)
    - These did not slow progression or change the disease course but improvement in quality of life could reduce stress and in turn slow the development of new brain lesions.
- Patient education, work adjustments, pacing, diet and exercise modifications, and environmental changes may be helpful enough to manage fatigue without the use of medications. (Khan et al., 2014)
    - Managing depression and eliminating unnecessary medications can minimize fatigue in the MS patient. (Khan et al. 2014)
- Aerobic and resistance exercise training in MS patients improved quality of life by improving balance, walking, decreased depression, and overall decreased disease severity. It is recommended to begin a steady level of physical activity early in the disease process to prevent disability and fatigue. (Grazioli et al., 2019)
    - It is recommended to exercise using cooling techniques, certain clothing, and choosing the coolest part of the day to limit the chances of increased body temperature. (Jain et al., 2020)

Pharmacological Treatment Methods

- Medications used in autoimmune diseases such as MS are called disease-modifying treatments (DMT's). They come in different forms and vary in efficacy depending on the patient. (See Figure A) (Khan et al., 2014)
    - Oral medications used for long term use in MS are teriflunomide, Monomethyl fumarate, Dimethyl fumarate, fingolimod, cladribine, Siponimod, diroximel fumarate, and ozanimod.
    - Injectable medications are interferon beta-1b's, glatiramer acetate, ofatumumab, peginterferon beta-1a's, and interferon beta-1a's.
    - IV infused medications include alemtuzumab, mitoxantrone, ocrelizumab, and natalizumab. (Khan et al., 2014)
- Up to 80% of people initially diagnosed with RRMS will convert to SPMS within 20 years. Research has shown that some DMT's are more effective than others in preventing RRMS from converting to SPMS, and that using any DMT prevented conversion better than choosing to use only nonpharmacological methods. (See Figure B)
    - The earlier a DMT is started after diagnosis or first sign of symptoms the less likely a patient is to convert from RRMS to SPMS. Within the first five years shows the best results. (Brown et al., 2019)
- Alemtuzumab, fingolimod, and dimethyl fumarate were the most effective treatment options for limiting disability. (Khan et al., 2014)
- Alemtuzumab is the DMT of choice for MS, however more affordable options with similar effects are interferon beta-1b, peg-interferon beta-1a, and natalizumab. (Khan et al. 2014)
- For relapse, high-dose methylprednisolone is recommended, at least 2,000 milligrams for no more than 31 days. There is no evidence that this treatment is more effective than choosing no treatment at all.
    - Other medical management options for relapse include plasmapheresis and adrenocorticotrophic hormone gel. (Caster & Edwards, 2015)
- Symptoms that can be managed with medication are bladder and bowel dysfunction, bladder infection, depression, emotional changes, dizziness, fatigue, itching, pain, tremors, spasticity, sexual problems, and problems with gait.

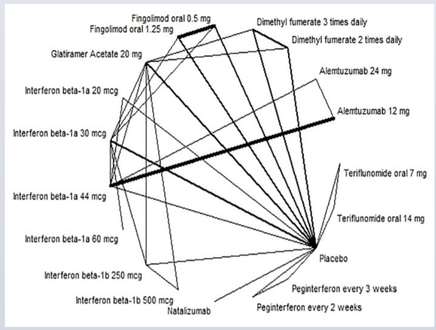


Figure A: Khan et al. (2014)

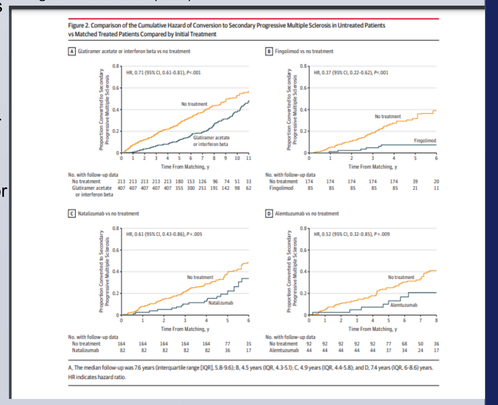
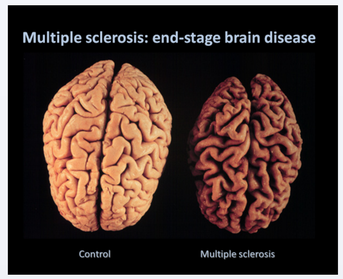


Figure B: Brown et al. (2019)



(WVE and Ireland, MS and ME, 2011=2014)

CONCLUSION

- It would be beneficial for all MS patients to begin taking a disease-modifying drug as close to diagnosis as possible. This is the best defense in preventing new brain lesions from forming and slowing the progression of disability. (Brown et al., 2019)
- The drug used most commonly is Alemtuzumab. (Hamidi, 2018)
- More cost effective treatment options include interferon beta-1b, peg-interferon beta-1a, and natalizumab. (Hamidi, 2018)
- Avoiding triggers and reducing stress would also benefit MS patients, by reducing the number of relapses and slowing disability in some instances. (Mohr, 2012)
- For severe relapses, short courses of methylprednisolone can be used, but if symptoms are manageable without treatment, that is the preferred option. (Caster & Edwards, 2015)
- Long term disease symptoms and drug side effects like fatigue and depression can be managed with other medications or therapies to improve quality of life. (Khan et al., 2014)
- Even though DMT's are proven to help MS patients, more than 25% of patients taking them do not adhere to their medication regimen well enough to be effective. (Hancock, 2011)
- It is important to be compliant with all treatment, pharmacologic and nonpharmacological, even in periods of remission. Brain lesions and damage cannot be reversed, only prevented.
    - DMT side effects are often limiting and considered a barrier to compliance. (Hancock, 2011)

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